REMARKS

By this amendment, Claims 1, 4-7, 18, and 20 are currently amended, Claims 2-3 and 9 remain as originally presented, Claims 8 and 19 are canceled, and Claims 10-17 were previously withdrawn.

The above-identified Office Action has been reviewed and the references carefully considered. In view hereof, the present amendment is submitted. It is contended that by the present amendment all bases of rejection set forth in the Office Action are traversed and overcome. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Acknowledgement of Co-pending Application

Pursuant to MPEP 2001.06(b), the Applicant is submitting herein a copy of the Office Action and the Applicant's response thereto in the Applicant's co-pending application (Serial No. 10/798,117). The enclosed Office Action was mailed on March 18, 2008.

In addition, along with the present Amendment the Applicant is contemporaneously submitting an Information Disclosure Statement. The IDS discloses the prior art cited in the March 18, 2008 Office Action in the co-pending application. More specifically, the IDS discloses U.S. Patent Nos. 6,040,147 and 6,723,348, as well as an article by Brian J. Lipworth, entitled "Allergic Inflammation in the unified airway: state with the nose."

Applicant's Claim of Priority

The Examiner has rejected the Applicant's claim of priority to U.S. Provisional Application Serial No. 60/453,917 for failure to maintain copendency between the current

and prior applications. The Applicant notes that the provisional application was filed more than one year before the filing of the present application. As such, the Applicant is presently submitting a new Declaration which does not claim the benefit of U.S. provisional application 60/453,917.

The Examiner has also rejected the Applicant's claim of priority to U.S. Application No. 10/798,117, arguing that the claimed invention of the present application is not disclosed in that application.

However, the Applicant respectfully contends that, under MPEP § 201.08, the Applicant is not required to withdraw the claim to priority, nor is the applicant required to identify portions of the previously-filed copending application which disclose the claimed invention of the present application. MPEP § 201.08 states that:

> ***Unless the filing date of the earlier nonprovisional application is actually needed***, for example, in the case of an interference or to overcome a reference, ***there is no need for the Office to make a determination as to whether*** the requirement of 35 U.S.C. 120, that ***the earlier nonprovisional application discloses the invention of the second application in the manner provided by the first paragraph of 35 U.S.C. 112***, is met and whether a substantial portion of all of the earlier nonprovisional application is repeated in the second application in a continuation-in-part situation. Accordingly, an alleged continuation-in-part application should be permitted to claim the benefit of the filing date of an earlier nonprovisional application if the alleged continuation-in-part application complies with the other requirements of 35 U.S.C. 120 and 37 C.F.R. 1.78, such as:
>
> (A) The first application and the alleged continuation-in-part application were filed with at least one common inventor;
>
> (B) The alleged continuation-in-part application was "filed before the patenting or abandonment of or termination

> of proceedings on the first application or an application similarly entitled to the benefit of the filing date of the first application:" and
>
> (C) The alleged continuation-in-part application "contains or is amended to contain a specific reference to the earlier filed application."

The Applicant notes that none of the references cited in the Examiner's Office Action may be overcome by the March 11, 2004 filing date of U.S. Application No. 10/798,117. Therefore, the Applicant respectfully contends that, according to MPEP § 201.08, it is improper to reject the Applicant's claim of priority to U.S. Application No. 10/798,117 because none of the references cited by the Examiner in the Office Action may be overcome by the previously-filed nonprovisional application.

Furthermore, the Applicant contends that the Applicant's claim of priority is proper because, as required by MPEP § 201.08: the applications have a common inventor; the applications are co-pending; and the application has been amended to contain a specific reference to the earlier filed application.

In addition, the Applicant respectfully contends that the claim of priority to U.S. Provisional Application Nos. 60/461,534 and 60/482,574 are proper and need not be withdrawn. Both provisional applications disclose the treatment of systemic inflammation and the resulting benefits. Application 60/461,534 discloses that a resulting benefit is that "eyes were dry" (paragraph [0027]). The claimed invention in the present application is directed towards reducing C-reactive protein associated with systemic inflammation. It is disclosed in the provisional application that the treatment has beneficial results for eyes as well. Therefore, the Applicant contends that the previously-filed provisional applications

disclose that the eyes benefit from the claimed method of treatment to the extent that the disorder associated with the eye is related to systemic inflammation.

Amendments to the Specification

The Examiner has objected to the Applicant's claim of priority due to an incorrect serial number identified in the first paragraph of the specification. The Applicant has amended the first paragraph of the specification to contain a proper claim of priority to the correction application serial number. Therefore, the Applicant respectfully requests that the Examiner withdraw this objection to the specification.

In addition, the Applicant has amended paragraphs [0017] and [0018]. The amendments to paragraphs [0017] and [0018] have been made so that the specification correctly reflects that Astelin® (azelastine) is an antihistamine and not a steroid. In addition, a minor amendment has been made to paragraph [0018] to correct the misspelling of "acetonide."

The Applicant respectfully contends that no new matter has been made by these amendments to the specification.

Claim Objections

Claims 5, 6, and 20 have been objected to due to misspelled words. Those informalities have been addressed, and proper amendments have been made to those claims.

Claim Amendments Not Initiated by Office Action

The Applicant notes that several claim amendments have been made which are not in direct response to the Examiner's Office Action. During prosecution of the co-pending application, it was determined that many of the listed compounds in Claim 4 are not

leukotriene inhibitors. Therefore, Claim 4 has been amended so as to eliminate any non-leukotriene inhibitors from the claim. In addition, Claims 5-7 and 20 contain amendments which are related to properly claiming azelastine as an antihistamine rather than as a steroid.

Claim Rejections 35 U.S.C. § 112, 1st Paragraph

The Examiner rejected Claims 1-9 and 18-20, arguing that the specification does not enable a person having ordinary skill in the art to make and use the invention commensurate in scope with those claims.

The Applicant notes that on page 4 of the Office Action, the Examiner states that "Applicant is enabled for those improvements of vision that are recognized by the art as treatable by a leukotriene inhibitor, an antihistamine and/or a corticosteroid . . . but not all ways in which vision may be improved." The Applicant has amended Claims 1 and 18 so that both independent claims are now directed towards a method for improving the vision of a user having an eye disorder attributable to systemic inflammation, wherein the user's vision is improved by reducing the C-reactive protein in the body of the user. It is now believed that the claims have been amended so as to comply with the Examiner's perceived scope of enablement of the specification. Therefore, the Applicant respectfully requests the Examiner withdraw this rejection of the claims.

Claim Rejections 35 U.S.C. § 112, 2nd Paragraph

The Examiner has rejected Claims 2-7 and 9 as being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicant regards as the invention. The Applicant has amended Claim 1 so that it is now directed to a composition consisting essentially of a leukotriene inhibitor, an antihistamine, and a

corticosteroid. The "and" which the Examiner stated is the source of indefiniteness has been deleted. Therefore, the Applicant contends that the rejection of Claims 2-7 and 9 for indefiniteness has been overcome, and the Applicant respectfully requests the Examiner to withdraw this rejection.

The Examiner has rejected Claims 2-9 and 20 as being indefinite because the claimed units for the corticosteroid are in μcg, rather than in units such as grams or milligrams. The Applicant respectfully contends μcg is a well-known unit in the area of pharmacology. 1 μcg is equivalent to 1 mcg (see attached Exh. A, on pages 4-5 these units are used interchangeably), and it is obvious to those of ordinary skill in the art that 1 μcg equals 1mcg. Furthermore, dosage amounts for the available corticosteroids are most often in the units of mcg (see Exh. B which states that the total daily recommended dose for Flonase® (fluticasone propionate) is 200 mcg). Therefore, mcg is a very common unit for dosage amounts of corticosteroids, and one of ordinary skill in the art knows that 1 μcg equals 1 mcg. As such, the Applicant respectfully contends that use of the unit "μcg" does not render a claim indefinite, and the Applicant respectfully requests that the Examiner withdraw this rejection of Claims 2-9 and 20.

The Examiner has further rejected Claims 1-9 as being indefinite for use of the phrase "highly sensitive C-reactive protein." The Applicant has amended Claim 1 so that it now states "C-reactive protein," and there is no longer any basis for indefiniteness regarding "highly sensitive" as set forth in the Examiner's Office Action. Therefore, the Applicant respectfully requests the Examiner withdraw this rejection of Claims 1-9.

The Examiner has also rejected Claims 1-9 as being indefinite for use of the phrase "at least about 2 days." The Applicant has amended Claim 1 to now state "at least 2 days." The Applicant contends that this basis of rejection has been overcome, and respectfully requests the Examiner withdraw this rejection of Claims 1-9.

Claim Rejections 35 U.S.C. § 102

The Examiner has rejected Claim 18 under 35 U.S.C. § 102(b) as anticipated by U.S. Patent No. 5,998,454 to Fleisch et al. Section 102(b) states that a person shall not be entitled to a patent when:

> the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Applicant traverses the Examiner's rejection. Under 35 U.S.C. § 102, to constitute an anticipation all the claimed elements must be found in exactly the same function and united in the same way to perform the identical function in a single unit of the prior art. Stated differently, anticipation can only be established by a single prior art reference which discloses each and every element of the claimed invention.

The Applicant has amended Claim 18 to now require a composition consisting essentially of a leukotriene inhibitor, an antihistamine, and a corticosteroid. The Applicant notes that, on page 14 of the Office Action, the Examiner states that "Fleisch et al. does not teach the use of antihistamines." As such, Fleisch does not disclose each and every element of Claim 18 as currently amended. Therefore, the Applicant respectfully requests the Examiner to withdraw this rejection of Claim 18.

The Examiner has rejected Claims 1 and 18 under 35 U.S.C. § 102(b) as anticipated by U.S. Patent No. 5,602,143 to Krauss. The Applicant has amended Claim 1 to now comprise the composition consisting essentially of a leukotriene inhibitor, and antihistamine, and a corticosteroid. The Applicant respectfully contends that Krauss does not teach the use of antihistamines. Therefore, Krauss does not disclose each and every element of Claims 1 or 18 as currently amended. As such, the Applicant respectfully requests the Examiner withdraw this rejection of Claims 1 and 18.

The Examiner has rejected Claims 1 and 18 under 35 U.S.C. § 102(e) as anticipated by U.S. Patent No. 6,635,654 to Chang et al. The Applicant respectfully contends that Chang does not teach the use of either a leukotriene inhibitor or a corticosteroid. Therefore, Chang does not teach each and every element of Claims 1 and 18, and withdrawal of this rejection is respectfully requested.

Claim Rejections 35 U.S.C. 103

The Examiner has set forth an extensive list of rejections under 35 U.S.C. § 103(a). A number of these rejections pertain to one or two of the compositions previously listed in the group of compounds in Claims 1 and 18. As discussed above, Claims 1 and 18 have now been amended to require all three compositions. As previously presented, only Claims 8 and 19-20 required all three compounds. Therefore, it is now believed that any basis of rejection which was not used to reject Claims 8, 19, or 20 has been overcome by the current amendments to Claims 1 and 18.

The following is a list of rejections which do not address the use of all three compositions, and are now believed to be overcome based upon the amendments to Claims 1 and 18:

1. The rejection of Claim 18 as being obvious over Fleisch.

2. The rejection of Claims 1 and 18 as being obvious over Fleisch in view of Chang.

3. The rejection of Claims 1-4 and 7 as being obvious over Fleisch and Chang in further view of U.S. Patent Application Publication 2003/0096840 to Down.

4. The rejection of Claims 1-3 and 7 as being obvious over Fleisch and Chang in further view of Dal Negro et al.

5. The rejection of Claims 1, 2, and 6 as being obvious over Fleisch, Chang, Dal Negro, and in further view of U.S. Patent No. 6,677,326 to Bardsley.

In light of the Applicant's amendments to Claims 1 and 18, the Applicant respectfully requests the Examiner withdraw the preceding rejections.

The Applicant will now address the rejections which do relate to the use of all three compositions.

The Examiner has rejected Claims 1-3, 5, 7, 18, and 19 under 35 U.S.C. § 103(a) as being obvious over Fleisch and Chang, and in further view of U.S. Patent No. 6,521,254 to Weinstein. 35 U.S.C. § 103(a) states that:

> [a] patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.

Applicant traverses the Examiner's rejection.

The Examiner contends that it would have been obvious to one of ordinary skill in the art to combine Fleisch and Chang to provide a composition consisting essentially of a leukotriene inhibitor, an antihistamine, and a corticosteroid. The Examiner's basis for this is that method of Fleisch treats the symptom while the method of Chang addresses the underlying cause.

The Applicant respectfully contends that it would not be obvious to one of ordinary skill in the art to combine Fleisch and Chang because the general theory of medical practice held by those having ordinary skill in the art is to reduce the number of medications prescribed to an individual. It is well known in the art that an increased number of medications to treat a single disorder is undesirable to the extent that the individual is exposed to an unnecessary increase in side effects. Fleisch even states that "overuse of corticosteroids has ominous side effects" (col. 1, lines 30-31).

Therefore, one having ordinary skill in the art would seek to reduce the number of medications prescribed for eliminating eye disorders relating to allergies due to the complications which arise from unnecessary medications.

Claims 1 and 18 are directed towards treating eye disorders due to systemic inflammation by reducing the C-reactive protein levels in the body of the user. Claims 1 and

18 are directed towards a treatment which operates in a different manner than that disclosed by Fleisch and Chang. One having ordinary skill in the art would not combine Fleisch and Chang due to the undesirable nature of increased and unnecessary medications. Conversely, in Claims 1 and 18, the claimed method operates by reducing the C-reactive proteins in the body, which has an effect of improving the user's vision. Therefore, it would not be obvious to one of ordinary skill in the art to combine Fleisch and Chang to provide a composition having an antihistamine, a leukotriene inhibitor, and a corticosteroid.

Furthermore, the Applicant respectfully contends that neither Fleisch nor Chang teach that C-reactive levels in the body are reduced.

The Examiner contends that Weinstein discloses dosages of antihistamines which are within the range claimed in Claims 1-3, 5, 7, 18, and 19. However, the Applicant respectfully contends that the claimed dosage levels for the leukotriene inhibitor and the corticosteroid are not taught by Fleisch, Chang, or Weinstein. Therefore, Fleisch, Chang, and Weinstein collectively fail to disclose each and every limitation found in Claims 1-3, 5, 7, 18, and 19. It would not be obvious to one of ordinary skill in the art to modify the combined teachings of the art references to teach the claimed invention. Therefore, the Applicant respectfully requests the Examiner withdraw the rejection of Claims 1-3, 5, 7, 18, and 19.

The Examiner has rejected Claims 1-5, 7-9, and 18-19 as being obvious over Fleisch, Chang, Weinstein, and in further view of Down and Dal Negro. The Applicant respectfully contends that, as a matter of law, the combination of any five references is not obvious. The fact that five references have been used is indicative that the Examiner has selectively chosen references to piece together the Applicant's claimed invention. The Applicant respectfully

contends that the use of five references is indicative that the claimed invention is indeed not obvious. Furthermore, the Applicant maintains that none of the five cited references discloses that C-reactive proteins are reduced, which in turn treats systemic inflammation, thereby improving the vision of a user who is inflicted with an eye disorder associated with systemic inflammation. Therefore, the Applicant respectfully requests that the Examiner withdraw this rejection of Claims 1-5, 7-9, and 18-19.

The Examiner has rejected Claims 1, 2, 6, 18, and 20 as being obvious over Fleisch, Chang, Weinstein, Down, Dal Negro, and in further view of U.S. Patent No. 6,677,326 to Bardsley. The Applicant respectfully contends that, as a matter of law, the combination of any six references is not obvious. The fact that six references have been used is indicative that the Examiner has selectively chosen references to piece together the Applicant's claimed invention. The Applicant respectfully contends that the use of six references is indicative that the claimed invention is indeed not obvious. Furthermore, the Applicant maintains that none of the six cited references discloses that C-reactive proteins are reduced, which in turn treats systemic inflammation, thereby improving the vision of a user who is inflicted with an eye disorder associated with systemic inflammation. Therefore, the Applicant respectfully requests that the Examiner withdraw this rejection of Claims 1, 2, 6, 18, and 20.

Applicant submits that the claims presented herein define patentably over the prior art of record herein.

Conclusion

It is respectfully submitted by this amendment that all bases of rejection and objection have been traversed and overcome and thus, it is contended that the application

has now been placed in a condition for allowance. A notice to this effect is, therefore, respectfully requested.

If the Examiner feels that prosecution of this application can be expedited, then she is courteously requested to place a telephone call to the Applicant's attorney at the number listed below.

Respectfully submitted,

Dated: 8/19/2008

David L. Oppenhuizen, Reg. No. 57562
The Weintraub Group, P.L.C.
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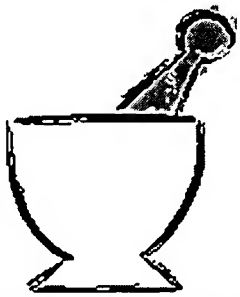
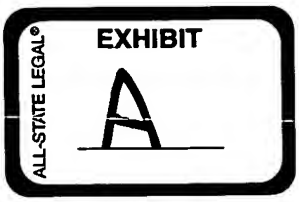
248-865-9430

ST VINCENT HOSPITAL PHARMACY





PHARMACISTS

- ***DRUG INFORMATION SITES***
  - CLINICAL PHARMACOLOGY 2000 -Accessible through any computer in our Hospital. No password required. **Find out IV compatibility information..... by clicking on the above link to get to the Clinical pharmacology database then click on the "Clinical Reports" tab, then click on the "IV Compatibility" link, then follow the online instructions on how to use the IV Compatibility module.**
  - CLINICAL REFERENCES - Our on-line clinical references. This link contains many links to medical information resources.
  - NEW MEXICO STATE BOARD OF PHARMACY
  - MEDSCAPE -Free drug information. Use user ID : stvinorg and Password: stvin
  - JOHN HOPKINS-ABXGUIDE -Free antibiotic information Use user ID : stvinorg and Password: stvin
  - TABLET IDENTIFICATION - A good free site to identify medications by the

imprint on the tablet

- FREE MEDLINE- INTERNET PUBMED
- RXFACTSTAT- Lots of free drug information can be found on this website
- THE NEW MEXICO POISON AND DRUG INFORMATION CENTER - Number to call when you need poison information, drug identification or drug information

- ***OUTPATIENT PHARMACY***

- NEW MEXICO BOARD OF PHARMACY SIGNIFICANT ADVERSE DRUG EVENT REPORTING FORM

- ***HIV NEEDLESTICK PROPHLAXIS***
  - DRUG REDIMEN FOR H.I.V. NEEDLESTICK PROPHALAXIS - ***Basic and Expanded Drug Regimens for HIV Postexposure Prophylaxis***

- ***DRUG SHORTAGES INFORMATION***

- DRUG SHORTAGES INFORMATION- U.S. Food and Drug Administration Center for Drug Evaluation and Research drug shortage page.
- AMERICAN SOCIETY OF HEALTH SYSTEM PHARMACIST DRUG SHORTAGE INFORMATION
- CORTICOID INJECTIONS SHORTAGE DOCUMENT- This document discusses recent shortages in corticoid injections and the alternatives for those that are in short supply
- GLUCOCORTICOID INJECTTIONS SHORTAGE DOCUMENT- This document discusses recent shortages in glucorticoid injections and the alternatives for those that are in short supply
- CEFOXITIN INJECTION SHORTAGE DOCUMENT - This document explains the use of a alternative to cefoxitin.

- ***ENTERAL FEEDINGS INFORMATION***
  - ENTERAL FEEDING CONTENTS -Gives the calories provided and the contents of the enteral feedings that the pharmacy department provides.
  - ENTERAL FEEDING SUBTITUTION GUIDE-Gives the contents of Enteral feedings. A guide that instructs you on what enteral feeding provided by pharmacy replaces a enteral feeding not provided by pharmacy.
  - NOVARTIS MEDICAL NUTRITION - The Novartis Enteral Product Reference Guide.

- ***CONSULT NOTES***
  - CEFOTETAN HYPOPROTHOMBINEMIA CHART NOTE [1]
  - LEVAQUIN IV TO P.O. CHART NOTE[1]
  - PROTONIX –vs- PRILOSEC CHART NOTE[1]
  - CLINICAL PHARMACY CONSULTATION NOTE BLANK[1]
  - DIGOXIN CONSULT NOTE: PATIENTS WITH RENAL IMPAIRMENT[1]
  - VANCOMYCIN CONSULTATION NOTE[1]
  - KETORALAC CONSULTATION NOTE[1]
  - CLINDAMYCIN CONSULTS[1]
  - CEFUROXIME RENAL NOTE[1]
  - UNASYN CONSULT NOTE[1]
  - PROCALAMINE CONSULT[1]

- ANTIVIRAL CONSULT[1]
- LOVENOX DVT CONSULT[1]
- QUINOLONE CONSULTATION[1]
- DIFLUCAN IV TO P.O.[1]
- LOVENOX 40MG QD[1]
- MEPERIDINE[1]
- SMX-TMP CONSULTS[1]

- ***USEFUL FORMULAS***
  - DIPYRIDAMOLE DOSING-[3] Table that tells you the dose of Dipyridamole based on weight (0.57mg/kg), tells how much to draw up and how much saline to use to make it to a volume of 40ml.
  - INTEGRILIN CALCULATOR- Answer Yes or No to the question "is the serum creatinine between 2 and 4" and input the patients weight and it will determine the dose d and the infusion drip rate in ml/hr . If serum creatinine is between 2 and 4 the drip rate is determined at 1 mcg/kg/min if the serum creatinine is ***not*** between 2 and 4 the drip rate is determined at 2mcg/kg/min. It also has some general information on Integrilin.
  - PEDIATRIC ADVANCE LIFE SUPPORT DRUG [3]-Input the patients age and weight and this table calculates the minimum and maximum dose of ADVANCED LIFE SUPPORT MEDICATION to use.
  - mcg/kg/min to mg/kg/hr Converter[1]- Given the weight of a patient

this calculator will determine the mcg/kg/min or mg/kg/hr or given the mcg/kg/min it will convert it to mg/kg/hr. The total dose in mcg or mg will also be calculated.

- DRIP RATE CALCULATOR mcg/kg/min- Given the dose in µcg/kg/min and it will determine the rate the drip should run in ml/hr

- DRIP RATE CALCULATOR mcg/min- Given the dose in µcg/min and it will determine the rate the drip should run in ml/hr

- STEROID EQUIVALENT DOSE CHART- A steroid dose conversion chart.

- ***PNT APPROVED PHARMACY DRUG PROTOCOLS***
  - HIGH RISK DRUG PROTOCOL[1]
  - MEDICATION ADMINISTRATION[1]
  - RENAL DOSING PROTOCOL[1]
  - IV TO PO PROTOCOL[1]
  - THERAPEUTIC SUBSTITUTION PROTOCOL[1]
  - CURRENT THERAPEUTIC SUBSTITUTION LIST[1]- Therapeutic substitutions currently in effect.
  - IV DRUG ADMINISTRATION POLICY [2]
  - ONCE A DAY AMINOGLYCOSIDE DOSING PROTOCOL
  - APPENDIX B OF THE AMINOGLYCOSIDE DOSING PROTOCOL
  - HINTS FOR THE AMINOGLYCOSIDE PROTOCOL
  - AMINOGLYCOSIDE WORKSHEET [2]

- TNKase PROTOCOL[1]
- INSULIN PROTOCOL

- ***INTRAVENOUS EXTRAVASTIONS GUIDELINES***
  - INTRAVENOUS EXTRAVASATIONS-A document that gives information on extravasations guidelines .

- ***P AND T COMMITEE INFORMATION***
  - XIGRIS® INFORMATION[1]
  - FENOLDOPAM MESYLATE (CORLOPAM®) INFORMATION[1]

- ***USEFUL PHARMACY FORMS AND DOCUMENTS***
  - PHARMACY INTERVENTIONS FORM[3]
  - LIST OF PROTOCOL MNEMONICS FOR MEDS-MANAGER[3]
  - LIST OF DRUG NAME MNEMONICS FOR MEDS-MANAGER-
  - REFRIGERATOR TEMP LOG[1]
  - 24 HOUR TPN WORKSHEET[3]
  - ANTESTHESIA NARCOTIC BOX FORM (STANDARD)[3]
  - ANESTESTHESIA NARCOTIC BOX FORM (3ML SUFENTA)[3]
  - NARCOTIC INVENTORY VERIFICATION FORM[3]
  - CRNA SIGN OUT LOG[3]
  - DOCTORS ANESTESTHESIA SIGN OUT LOG[3]
  - OB ANESTESTHESIA NARCOTIC FORM [3]
  - CHARGE PHARMACIST DUTY CHECKLIST[3]

- PHARMACY TECH. DUTY SCHEDULE[3]
- 2ND FLOOR DECENTRALIZED PHARMACIST CHECKLIST[3]
- 3RD FLOOR DECENTRALIZED PHARMACIST CHECKLIST[3]
- UNIT INSPECTION FORM ONLINE - Submit your unit inspection form online.
- UNIT INSPECTION FORM-Print version of unit inspection form.
- PYXIS AUTHORIZATION FORMS
- CLINICAL MONITORING FORMS
- INSTRUCTIONS FOR THE DECENTRALIZED PHARMACIST PAGERS
- TPN SCALE CALIBRATION LOG FORM

- ***PHARMACY C.E. SITES***
  - FREE C.E. FROM POWER PAK
  - DRUG TOPICS CE
  - MEDSCAPE C.E.
  - UNIVERSITY OF KENTUCKY C.E.
  - RXFACTSTAT

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Flonase

Flonase Information

Generic Name: Fluticasone Propionate

Flonase (fluticasone propionate) nasal spray is indicated for the management of the nasal symptoms of seasonal and perennial allergic and nonallergic rhinitis in adults and pediatric patients 4 years of age and older.

Safety and effectiveness of Flonase (fluticasone propionate) nasal spray in children below 4 years of age have not been adequately established.

Flonase Ingredients and Composition

How Does Flonase Work?

Flonase (fluticasone propionate) is a synthetic, trifluorinated corticosteroid with anti-inflammatory⊞ activity. In vitro dose response studies on a cloned human glucocorticoid receptor system involving binding and gene expression afforded 50% responses at 1.25 and 0.17 nM concentrations, respectively. Fluticasone propionate was threefold to fivefold more potent than dexamethasone in these assays. Data from the McKenzie vasoconstrictor assay in man also support its potent glucocorticoid activity.

In preclinical studies, Flonase revealed progesterone-like activity similar to the natural hormone. However, the clinical significance of these findings in relation to the low plasma levels is not known.

The precise mechanism through which Flonase (fluticasone propionate) affects allergic rhinitis symptoms is not known. Corticosteroids have been shown to have a wide range of effects on multiple cell types (e.g., mast cells, eosinophils, neutrophils, macrophages, and lymphocytes) and mediators (e.g., histamine, eicosanoids, leukotrienes, and cytokines) involved in inflammation. In seven trials in adults, fluticasone propionate nasal spray has decreased nasal mucosal eosinophils in 66% (35% for placebo) of patients and basophils in 39% (28% for placebo) of patients. The direct relationship of these findings to long-term symptom relief is not known.

Fluticasone propionate nasal spray, Flonase, like other corticosteroids, is an agent that does not have an immediate effect on allergic symptoms. A decrease in nasal symptoms has been noted in some patients 12 hours

after initial treatment with fluticasone propionate nasal spray. Maximum benefit may not be reached for several days. Similarly, when corticosteroids are discontinued, symptoms may not return for several days.

How To Take Flonase and Flonase Dosage and Administration

Patients should use Flonase (fluticasone propionate) nasal spray at regular intervals as directed since its effectiveness depends on its regular use.

Adults:

The recommended starting Flonase dosage in adults is two sprays (50 mcg of fluticasone propionate each) in each nostril once-a-day (total daily dose, 200 mcg). The same dosage divided into 100 mcg given twice-a-day (e.g., 8 a.m. and 8 p.m.) is also effective. After the first few days, patients may be able to reduce their dosage to 100 mcg (one spray in each nostril) once daily for maintenance therapy.

Adolescents and Children (4 Years of Age and Older):

Patients should be started with 100 mcg of Flonase (one spray in each nostril once-a-day). Patients not adequately responding to 100 mcg may use 200 mcg (two sprays in each nostril). Once adequate control is achieved, the dosage should be decreased to 100 mcg (one spray in each nostril) daily.

The maximum total daily dosage should not exceed two Flonase sprays in each nostril (200 mcg per day).

Flonase (fluticasone propionate) nasal spray is not recommended for children under 4 years of age.

Directions for Use:

Illustrated patient's instructions for proper use accompany each package of Flonase nasal spray.

If you suspect a Flonase Overdose

Chronic overdosage with Flonase (fluticasone propionate) nasal spray may result in signs/symptoms of hypercorticism. Intranasal administration of 2 mg (10 times the recommended dose) of fluticasone propionate twice daily for 7 days to healthy human volunteers was well tolerated. Single oral doses of Flonase of up to 16 mg have been studied in human volunteers with no acute toxic effects reported. Repeat oral doses up to 80 mg daily for 10 days in volunteers and repeat oral doses up to 10 mg daily for 14 days in patients were well tolerated. Adverse reactions were of mild or moderate severity, and incidences were similar in active and placebo treatment groups. Acute overdosage with this dosage form is unlikely since one bottle of fluticasone propionate nasal spray contains approximately 8 mg of fluticasone propionate.

The oral and subcutaneous median lethal Flonase doses in mice and rats were >1000 mg/kg (>20,000 and >41,000 times, respectively, the maximum recommended daily intranasal dose in adults and >10,000 and >20,000 times, respectively, the maximum recommended daily intranasal dose in children on a mg/m2 basis).

Flonase Side Effects

Flonase Precautions and Contraindications

General:

Rarely, immediate hypersensitivity reactions or contact dermatitis may occur after the administration of Flonase (fluticasone propionate) nasal spray. Rare instances of wheezing, nasal septum perforation, cataracts, glaucoma and increased intraocular pressure have been reported following the intranasal application of corticosteroids, including fluticasone propionate.

Use of excessive doses of corticosteroids such as Flonase may lead to signs or symptoms of hypercorticism, suppression of HPA function, and/or reduction of growth velocity in children or teenagers. Physicians should closely follow the growth of children and adolescents taking corticosteroids, by any route, and weigh the benefits of corticosteroid therapy against the possibility of growth suppression if growth appears slowed.

Although systemic effects have been minimal with recommended doses of fluticasone propionate nasal spray, potential risk increases with larger doses. Therefore, larger than recommended doses of Flonase (fluticasone propionate) nasal spray should be avoided.

When used at higher than recommended doses, or in rare individuals at recommended doses, systemic corticosteroid effects such as hypercorticism and adrenal suppression may appear. If such changes occur, the dosage of Flonase (fluticasone propionate) nasal spray should be discontinued slowly consistent with accepted procedures for discontinuing oral corticosteroid therapy.

In clinical studies with Flonase (fluticasone propionate) administered intranasally, the development of localized infections of the nose and pharynx with Candida albicans has occurred only rarely. When such an infection develops, it may require treatment with appropriate local therapy and discontinuation of treatment with Flonase (fluticasone propionate) nasal spray. Patients using Flonase (fluticasone propionate) nasal spray over several months or longer should be examined periodically for evidence of Candida infection or other signs of adverse effects on the nasal mucosa.

Flonase (fluticasone propionate) nasal spray should be used with caution, if at all, in patients with active or quiescent tuberculous infection; untreated local or systemic fungal or bacterial, or systemic viral infections

or parasitic infection; or ocular herpes simplex.

Because of the inhibitory effect of corticosteroids on wound healing, patients who have experienced recent nasal septal ulcers, nasal surgery, or nasal trauma should not use a nasal corticosteroid such as Flonase until healing has occurred.

Flonase Drug Interactions

In a placebo-controlled, crossover study in eight healthy volunteers, coadministration of a single dose of orally inhaled Flonase (fluticasone propionate) (1000 mcg, 5 times the maximum daily intranasal dose) with multiple doses of ketoconazole (200 mg) to steady state resulted in increased mean fluticasone propionate concentrations, a reduction in plasma cortisol AUC, and no effect on urinary excretion of cortisol. This interaction may be due to an inhibition of the cytochrome P450 3A4 isoenzyme system by ketoconazole, which is also the route of metabolism[⊞] of fluticasone propionate. No drug interaction studies have been conducted with Flonase (fluticasone propionate) nasal spray; however, care should be exercised when fluticasone propionate is coadministered with long-term ketoconazole and other known cytochrome P450 3A4 inhibitors.

Flonase Clinical Trials and Studies

Storing Flonase

Storage: Store between 4-30°C (39-86°F).

Buy Flonase

Anti Inflammatory

Accutane Allegra Bextra Celebrex Flonase Guggulsterone Mobic Vioxx

Anti-Allergy and Allergy Relief

Alavert Allegra Claritin Flonase Nasonex Zyrtec

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/798,117	03/11/2004	John P. Mullally	MUJ-104-A	8807

7590 03/18/2008

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EXAMINER	
JAGOE, DONNA A	
ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
03/18/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/798,117	MULLALLY, JOHN P.	
	Examiner	Art Unit	
	Donna Jagoe	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *10-13 and 15-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☒ Claim(s) *5-7 and 14* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I in the reply filed on October 29, 2007 is acknowledged. The traversal is on the ground(s) that both the group I and II inventions are classified in the same class and subclass. Applicant asserts that it would not be an additional burden on the Examiner to search both groups at the same time. This is not found persuasive because these inventions are distinct/unrelated for the reasons in the restriction requirement dated September 25, 2007 and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper. Moreover, because a search of each distinct/unrelated invention would not be coextensive with the other(s), and because each invention will require its own separate patentability analysis, an examination and search of multiple inventions in a single application would constitute a serious undue burden on the examiner.

It should be remembered that the purpose of an election of species requirement is to simplify the search and issues considered during prosecution, and that because this is so the ultimate allowance of a generic claim will encompass all additional species within the scope of the allowed genus. Stated alternatively, the purpose of an election of species requirement, as opposed to a restriction between claim groups, is to reduce the burden on the examiner during prosecution only; a full search is merely postponed until allowance of the generic claim.

The requirement is still deemed proper and is therefore made FINAL.

Claims 10-13 and 15-20 are **withdrawn** from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on October 29, 2007.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claims 1-9 and 14 are presented for examination.

Claim Objections

Claim 5 is objected to because of the following informalities: the word loratadine is misspelled. Appropriate correction is required.

Claim 6 is objected to because of the following informalities: the word acetonide is misspelled. Further, there is a misplaced comma. It appears that acetoniode (sic) is a separate agent, however, the specification, on page 5, paragraph 19 states that the agent is triamcinolone acetonide, not triamcinalone, acetoniode (sic). Appropriate correction is required.

Claim 7 is objected to because of the following informalities: the word fluticasone is misspelled. Appropriate correction is required.

Applicant is advised that should claim 5 be found allowable, claim 14 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4, 6, 7 and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). The term "leukotriene inhibitor" in claim 4 is used by the claim to mean a plethora of antibiotics, steroids, theophylline, vaccine and other miscellaneous drug categories, while the accepted meaning is "montelukast and zafirlukast." The term is indefinite because the specification does not clearly redefine the term.

The term "antihistamine" in claim 6 is used by the claim to mean "mometasone furoate monohydrate, triamcinalone, acetoniode, budesonide and azelastine", while the accepted meaning is "azelastine." The term is indefinite because the specification does not clearly redefine the term. Azelastine is the only agent is this Markush group that is actually an antihistamine.

Claim 7 is rejected because the examples set forth in the specification are insufficient to justify the scope of the claim. The instant specification, at page 5, paragraph 21 gives support for each of the antihistamines to be administered in the alternative. The claim is drafted so that it appears that all of the antihistamines are administered together. Correction is required.

Claim 8 is rejected because it is a dependent claim that fails to disclose which claim it depends from rendering the scope of the claim indeterminate.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Lipworth et al. (U).

Lipworth et al. teach that there is an association between allergic inflammation in the upper airway and the lower airway and up to 40% of patients with asthma have allergic rhinitis and vise versa and since one will affect the other, neither condition should be treated in isolation (page 878, column 1, 1st paragraph).

Further, Lipworth et al. teach administration of leukotriene inhibitors such as montelukast and zafirlukast along with loratadine (page 878, column 2) and propose treatment options to include the use of the combined mediator blockade (antihistamine and leukotriene inhibitor) to facilitate the use of lower maintenance doses of topical corticosteroid. Recited corticosteroids include budesonide and mometasone (page 879, column 1).

Regarding the reduction of C-reactive protein, the recitation of the treatment of individuals "in need" of the treatment of a certain condition is missing. A physician will typically examine many patients with various pathologies, and only some will have a particular disease requiring a particular treatment. It has been traditional in United States practice to recite the treatment of individuals "in need" of the treatment of a certain condition so as to indicate that particular subset of patients actually in need of intervention; an alternative is to recite the treatment of an individual "suffering from" a given disease. Accordingly, the following format is preferred for claiming methods of treating: "A method for treating disease X comprising administering to an individual suffering from/in need of such treatment an effective amount of agent Y". Claims not specifying the subset of patients to be treated in this manner are generally viewed as being anticipated by any prior art method using a given agent since they read on administration to the general population and not a specified subset requiring treatment.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-9 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lipworth et al. (U), Ridker et al. U.S. Patent No. 6,040,147 A and Faham et al. U.S. Patent No. 6,723,348 B2.

Lipworth et al. teach that there is an association between allergic inflammation in the upper airway and the lower airway and up to 40% of patients with asthma have allergic rhinitis and vise versa and since one will affect the other, neither condition should be treated in isolation (page 878, column 1, 1st paragraph).

Further, Lipworth et al. teach administration of leukotriene inhibitors such as montelukast and zafirlukast along with loratadine (page 878, column 2) and propose treatment options to include the use of the combined mediator blockade (antihistamine and leukotriene inhibitor) to facilitate the use of lower maintenance doses of topical

corticosteroid. Recited corticosteroids include budesonide and mometasone (page 879, column 1). Lipworth teach effective doses of leukotriene inhibitor (montelukast 10 mg/day) and cetirizine (10 mg/day) as well as budesonide and mometasone 400µg daily and 200 µg daily (page 879, column 1).

It differs in that Lipworth et al. does not teach the reduction of C-reactive protein. Ridker et al. teach that C-reactive protein is a marker for underlying systemic inflammation (column 1, lines 60-61). It would have been obvious to employ the leukotriene inhibitors, antihistamines and corticosteroids of Lipworth et al. to reduce C-reactive protein in the body of the user motivated by the teaching of Lipworth that there is an association between allergic inflammation in the upper and lower airway and the teaching of Ridker et al. that C-reactive protein is a marker for underlying systemic inflammation. As such, as the inflammation is reduced, the C-reactive protein level would be reduced.

Regarding the fexofenadine of instant claim 7 and antihistamine dosages recited in claims 2 and 3, Faham et al. teach fexofenadine is an antihistamine (column 1, lines 28-30) and is administered in doses of from about 10 mg to about 500 mg/day (column 8, lines 36-47). This amount overlaps and encompasses the claimed amount of about 150 to about 250 mg. A *prima facie* case of obviousness exists where the claimed ranges are close enough that one skilled in the art would have expected them to have the same properties.

Regarding the combination of antihistamines in instant claim 7, as stated in In re Kerkhoven, 626 F.2d 846, 205 USPQ 1069, at page 1072 (CCPA 1980):

It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition which is to be used for the very same purpose. In re Susi, 58 CCPA 1074, 1079-80, 440 F.2d 442, 445, 169 USPQ 423, 426 (1971); In re Crockett, 47 CCPA 1018, 1020-21, 279 F.2d 274, 276-77, 126 USPQ 186, 188 (CCPA 1960). As this court explained in Crockett, the idea of combining them flows logically from their having been individually taught in the prior art.

Regarding the amount of corticosteroid in instant claims 2 and 3, Lipworth disclose 200 and 400 µg/day. The specific safe and effective amount will be vary, with such factors as the particular condition being treated, the physical condition of the patient, the duration of treatment , the nature of the concurrent therapy (if any), the specific dosage form to be used, the carrier employed, the solubility of the formula therein and the dosage regimen desired for the composition. As such, it would have been made obvious to one of ordinary skill in art at the time it was made to employ the recited amounts of corticosteroid motivated by the teaching of Lipworth et al. that dosages of corticosteroids can be lower when combined with a leukotriene inhibitor and an antihistamine for allergic inflammation.

Regarding claim 6, the nasal antihistamine, azelastine is disclosed in Lipworth et al. for the treatment of rhinitis.

Regarding claim 7, Ridker et al. teach fluticasone as an anti-inflammatory agent useful for reducing C-reactive protein (column 7, line 30).

Regarding the administration of the leukotriene and antihistamine orally and the steroid nasally infused, Lipworth et al. teach that treatment of allergic airway inflammation in the nose with topical corticosteroids may be associated with a commensurate improvement in bronchial hyper responsiveness and asthma control

(page 878, column 1). Oral leukotriene inhibitors and loratadine are also disclosed (page 878, column 2).

Thus the claims fail to patentably distinguish over the state of the art as represented by the cited references.

Accordingly, for the above reasons, the claims are deemed properly rejected and none are allowed.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (571) 272-0576. The examiner can normally be reached on Monday through Friday from 8:00 A.M. - 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

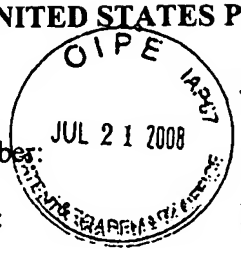
Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Donna Jagoe /D. J./
Examiner
Art Unit 1614

March 3, 2008

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE



Applicant:	John P. Mullally
Serial Number:	10/798,117
Filing Date:	March 11, 2004
Group Art Unit:	1614
Confirmation No.	8807
Examiner:	Donna A. Jagoe
Title:	**COMPOSITION AND METHOD FOR TREATING INFLAMMATIONS BY REDUCING C-REACTIVE PROTEIN**
Atty. Docket No.:	MUJ-104-A

AMENDMENT UNDER 37 CFR 1.111

Mail Stop: Amendment
Hon. Commissioner of Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Madam:

In response to the Office Action of March 18, 2008, please enter the following Amendment with respect to the above-identified application:

SPECIFICATION

Please replace paragraphs [0021] – [0022] with the following amended paragraph:

[0021] The antihistamine can be any of those which are commercially available such as those sold under the name "Zyrtec®" (cetirizine), "Allegra®" (fexodenadine), "Claritin®" (loratadine), ~~and~~ "Clarinex®" (desloratadine), and "Astelin®" (azelastine).

[0022] The nasal steroid is, preferably, fluticasone propionate. This propionate is sold commercially under the name "Flonase®." Other useful nasal steroids are those sold commercially under various trademarks such as, for example, "Nasonex®" (mometasone furoate monohydrate), "Nasacort AQ®" (triamcinolone acetoniode), and "Rhinocort Aqua®" (budesonide), ~~and "Astelin®" (azelastine),~~ to name a few.

CLAIMS

1. **(Currently Amended)** A method for treating users having systemic inflammation which comprises:

administering on a daily basis for a period of at least about 2 days, a composition selected from the group consisting of:

(a) from about 1 to about 20 milligrams of a leukotriene inhibitor,

(b) from about 150 to about 250 milligrams of an antihistamine,

(c) from about 110 µcg to about 220 µcg of a corticosteroid and,

(d) mixtures thereof

to reduce highly sensitive C-reactive protein in the body of the user.

2. **(Canceled)** The method of claim 1 wherein the selected composition is used in an amount of :

(d) from about 1 to about 20 milligrams of leukotriene inhibitor,

(e) from about 150 to about 250 milligrams of antihistamine, and

(f) from about 110 µcg to about 220 µcg of corticosteroid.

3. **(Currently Amended)** The method of claim ~~2~~ 1 wherein the selected composition is used in an amount of:

(a) from about 5 to about 15 milligrams of the leukotriene inhibitor,

(b) from about 175 to about 200 milligrams of the antihistamine, and

(c) from about 110 µcg to about 220µcg of the corticosteroid.

4. **(Currently Amended)** The method of claim ~~2~~ 1 wherein the leukotriene inhibitor is selected from the group consisting of:

~~albuterol sulfate, aminophylline, amoxicillin, ampicillin, astemizole, attenuated tubercle bacillus, azithromycin, bacampicillin, beclomethasone dipropionate, budesonide, bupropion hydrochloride, cefaclor, cefadroxil, cefixime, cefprozil, cefuroxime axetil, cephalexin, ciprofloxacin hydrochloride, clarithromycin, clindamycin, cloxacillin, doxycycline, erythromycin, ethambutol, fenoterol hydrobromide, fluconazole, flunisolide, fluticasone propionate, formoterol fumarate, gatifloxacin, influenza virus vaccine, ipratropium bromide, isoniazid, isoproterenol hydrochloride, itraconazole, ketoconazole, ketotifen, levofloxacin, minocycline,~~ montelukast sodium, ~~moxifloxacin, nedocromil sodium, nicotine, nystatin, ofloxacin, orciprenaline, oseltamivir, oseltamivir sulfate, oxtriphylline, penicillin, pirbuterol acetate, pivampicillin, pneumococcal conjugate vaccine, pneumococcal polysaccharide vaccine, prednisone, pyrazinamide, rifampin, salbutamol, salmeterol xinafoate, sodium cromoglycate (cromolyn sodium), terbutaline sulfate, terfenadine, theophylline, triamcinolone acetonide,~~ zafirlukast, ~~zanamivir,~~ zileuton and mixtures thereof.

5. **(Currently Amended)** The method of claim ~~2~~ 1 wherein the antihistamine is selected from the group consisting of:

cetirizine, fexofenadine, ~~and lortadine~~ loratadine, and azelastine.

6. **(Currently Amended)** The method of claim ~~2~~ 1 wherein the ~~antihistamine~~ corticosteroid is selected from the group consisting of:

mometasone furoate ~~mononhydrate~~ monohydrate, triamcinalone, ~~acetoniode~~ acetonide, and budesonide ~~and azelastine~~.

7. **(Currently Amended)** The method of claim ~~2~~ 1 wherein:

(a) the leukotriene inhibitor is montelukast sodium,

(b) the antihistamine is cetirizine, ~~fexofenadine and loratadine,~~ and

(c) the steroid is ~~fluticosone~~ fluticasone propionate.

8. **(Currently Amended)** The method of claim [[____]] 1 wherein the composition comprises:

(a) the leukotriene inhibitor,

(b) the antihistamine, and

(c) the corticosteroid.

9. **(Currently Amended)** The method of claim ~~2~~ 1 wherein:

the leukotriene and the antihistamine are administered orally and the steroid is nasally infused.

10. **(Withdrawn)** A composition for reducing C-reactive protein to treat systemic inflammation, consisting essentially of:

(a) a leukotriene inhibitor,

(b) an antihistamine, and

(c) a corticosteroid.

11. **(Withdrawn)** The composition of claim 10 wherein the composition comprises:

(g) from about 1 to about 20 milligrams of the leukotriene inhibitor,

(h) from about 150 to about 250 milligrams of antihistamine, and

(i) from about 110 μcg to about 220 μcg of corticosteroid.

12. **(Withdrawn)** The composition of claim 11 wherein the composition comprises:

(d) from about 5 to about 15 milligrams of leukotriene inhibitor,

(e) from about 175 to about 200 milligrams of antihistamine, and

(f) from about 110 μcg to about 220μcg of corticosteroid.

13. **(Withdrawn)** The composition of claim 11 wherein the leukotriene inhibitor is selected from the group consisting of:

albuterol sulfate, aminophylline, amoxicillin, ampicillin, astemizole, attenuated tubercle bacillus, azithromycin, bacampicillin, beclomethasone dipropionate, budesonide, bupropion hydrochloride, cefaclor, cefadroxil, cefixime, cefprozil, cefuroxime axetil, cephalexin, ciprofloxacin hydrochloride, clarithromycin, clindamycin, cloxacillin, doxycycline, erythromycin, ethambutol, fenoterol hydrobromide, fluconazole, flunisolide, fluticasone propionate, formoterol fumarate, gatifloxacin,

influenza virus vaccine, ipratropium bromide, isoniazid, isoproterenol hydrochloride, itraconazole, ketoconazole, ketotifen, levofloxacin, minocycline, montelukast sodium, moxifloxacin, nedocromil sodium, nicotine, nystatin, ofloxacin, orciprenaline, oseltamivir, oseltamivir sulfate, oxtriphylline, penicillin, pirbuterol acetate, pivampicillin, pneumococcal conjugate vaccine, pneumococcal polysaccharide vaccine, prednisone, pyrazinamide, rifampin, salbutamol, salmeterol xinafoate, sodium cromoglycate (cromolyn sodium), terbutaline sulfate, terfenadine, theophylline, triamcinolone acetonide, zafirlukast, zanamivir, and mixtures thereof.

14. **(Canceled)** The method of claim 2 wherein the antihistamine is selected from the group consisting of:

cetirizine, fexofenadine and lortadine.

15. **(Withdrawn)** The composition of claim 11 wherein the antihistamine is selected from the group consisting of:

(a) mometasone furoate mononhydrate,

(b) triamcinalone,

(c) acetoniode,

(d) budesonide, and

(e) azelastine.

16. **(Withdrawn)** The composition of claim 11 wherein:

(a) the leukotriene is montelukast sodium,

(b) the antihistamine is cetirizine, fexofenadine and loratadine, and

(c) the steroid is fluticosone propionate.

17. **(Withdrawn)** The composition of claim 16 wherein:

the leukotriene and the antihistamine are administered orally and the steroid is nasally infused.

18. **(Withdrawn)** A method for reducing sinus inflammation by reducing highly sensitive C-reactive protein to reduce systemic inflammations in the body of a user, comprising:

Administering on a daily basis a composition selected from the group consisting of:

(a) a leukotriene inhibitor,

(b) an antihistamine,

(c) a corticosteroid, and

(d) mixtures thereof.

19. **(Withdrawn)** The method of claim 18 wherein:

the composition is a mixture of the inhibitor, the antihistamine, and the corticosteroid.

20. **(Withdrawn)** The method of claim 19 wherein:

(a) the leukotriene inhibitor is a montelukast sodium present in an amount ranging from about 5 to about 15 milligrams,

(b) the antihistamine is selected from the group consisting of cetirizene, fexofenadine and lortadine present in an amount ranging from about 175 to about 200 milligrams, and

(c) the steroid is selected from the group consisting of:

momeasone furoate monohydrate, triamcinalone, acetoniode, budesonide, and azelastine, the steroid being present in an amount ranging from about 110 μcg to about 220 μcg.

REMARKS

By this amendment, Claims 1 and 3-9 are currently amended, Claims 2 and 14 are canceled, and Claims 10-13 and 15-20 were previously withdrawn.

The above-identified Office Action has been reviewed and the references carefully considered. In view hereof, the present amendment is submitted. It is contended that by the present amendment all bases of rejection set forth in the Office Action are traversed and overcome. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Amendments to the Specification

The Applicant is submitting amended paragraphs [0021] and [0022] to the specification. The amended paragraphs correct azelastine's designation as an antihistamine rather than as a steroid.

Claim Objections

Claims 5, 6, 7, and 14 have been objected to. The misspelled words in Claims 5-7 have been corrected. In addition, Claim 14, which was a duplicate of Claim 5, has now been canceled.

Claim Rejections 35 U.S.C. § 112

The Examiner rejected Claims 4, 6, 7, and 8 as being indefinite for failing to particularly point out and distinctly claim the subject matter.

Claim 4 has been amended so that the remaining group of leukotriene inhibitors includes only claim terms which refer to leukotriene inhibitors.

Claim 6 has been amended so that the claim is now directed towards corticosteroids rather than antihistamines. In addition, azelastine has been removed from the claim group as

azelastine is an antihistamine rather than a corticosteroid. The remaining claim terms are corticosteroids.

Claim 7 has been amended so that it now only refers to a single antihistamine.

Claim 8 has been amended so that it now is dependent upon Claim 1.

As such, the Applicant contends that the Examiner's bases for rejecting Claims 4, 6, 7, and 8 under 35 U.S.C. § 112 have been overcome. The Applicant respectfully requests the Examiner to withdraw these bases of rejection.

Claim Rejections 35 U.S.C. § 102(b)

The Examiner has rejected Claims 1, 4, and 5 under 35 U.S.C. § 102(b) as anticipated by Lipworth et al. Section 102(b) states that a person shall not be entitled to a patent when:

> the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Applicant traverses the Examiner's rejection. Under 35 U.S.C. § 102, to constitute an anticipation all the claimed elements must be found in exactly the same function and united in the same way to perform the identical function in a single unit of the prior art. Stated differently, anticipation can only be established by a single prior art reference which discloses each and every element of the claimed invention.

Applicant respectfully submits that Lipworth does not disclose each and every element required by the claims of Applicant's invention. Accordingly, Lipworth fails as a reference upon which to predicate an anticipation rejection and submits that the Examiner's rejection under § 102 should be withdrawn.

In an effort to expedite and facilitate prosecution, and acting without prejudice, the Applicant has amended Claim 1. The currently amended Claim 1 now includes the limitations

previously presented in Claim 2. In addition, Claim 1 has been amended so that it is now directed towards "treating users having systemic inflammation" to reduce highly sensitive C-reactive protein in the user's body.

Applicant contends that Lipworth does not teach the concomitant use of a leukotriene inhibitor, an antihistamine, and a corticosteroid for the purpose of reducing highly sensitive C-reactive protein levels in the body. Lipworth states that it would be an "intriguing possibility" to combine the leukotriene inhibitor and the antihistamine with a corticosteroid for the purpose of possibly "facilitat[ing] the use of lower maintenance doses of topical corticosteroid, thus optimising (sic) the therapeutic ratio and avoiding the potential for systemic adverse effects in susceptible patients." Thus, Lipworth states that the use of the corticosteroid with the combined mediator blockade is only an "intriguing possibility in treating rhinitis." Moreover, Lipworth does not teach or suggest doing so for the purpose of reducing C-reactive protein levels in the body. Furthermore, the Examiner admits as such on page 8 of the Office Action. "Lipworth et al. does not teach the reduction of C-reactive protein."

As such, Lipworth fails to disclose each and every element of Claim 1. Consequently, the Applicant respectfully requests the Examiner withdraw the rejection of Claim 1.

Applicant submits that Claim 1 is patentable over the prior art and in condition for allowance.

Claims 4 and 5 are dependent upon Claim 1, and therefore the Applicant contends that Claims 4 and 5 are allowable for the same reasons as stated above. Therefore, the applicant respectfully requests the Examiner withdraw the rejection of Claims 4 and 5.

Claim Rejections 35 U.S.C. 103

The Examiner has rejected Claims 1-9 and 14 under 35 U.S.C. § 103(a) as being obvious over Lipworth in view of U.S. Patent No. 6,040,147 to Ridker et al., and in further view of U.S. Patent No. 6,723,348 to Faham et al. 35 U.S.C. § 103(a) states that:

> [a] patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.

Applicant traverses the Examiner's rejection.

The Applicant maintains and the Examiner has conceded that Lipworth does not teach the combination of a corticosteroid with a leukotriene inhibitor and an antihistamine for reducing the levels of highly sensitive C-reactive protein in the body of a user. Furthermore, Ridker and Faham do not teach or suggest the combination of a corticosteroid with a leukotriene inhibitor and an antihistamine for such, nor in the amounts set forth in Claim 1. As such, Lipworth, Ridker, and Faham fail to collectively teach or suggest Claim 1. Therefore, Lipworth, Ridker, and Faham fail to collectively teach or suggest any claims which are dependent upon Claim 1. Claims 3-9 are presently amended so as to be dependent upon Claim 1 and include the limitations thereof.

Because Lipworth, Ridker, and Faham do not teach or suggest the subject matter of Claim 1. Necessarily, Claims 3-9 are patentably distinct therefrom. Accordingly, Applicant respectfully requests the Examiner withdraw the rejection of Claims 3-9.

Applicant submits that the claims presented herein define patentably over the prior art of record herein.

Conclusion

It is respectfully submitted by this amendment that all bases of rejection and objection have been traversed and overcome and thus, it is contended that the application has now been placed in a condition for allowance. A notice to this effect is, therefore, respectfully requested.

If the Examiner feels that prosecution of this application can be expedited, then he is courteously requested to place a telephone call to the Applicant's attorney at the number listed below.

Respectfully submitted,

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